

New pyrrolidone, imidazolone, furanon or thiophenone derivativ s

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Abstract

5-Membered azacyclic derivatives (I) and their salts are new. W = C(R<16>)-D-B-A-R<1> (a), C=C(R<16>)-D-B-A-R<1> (b) or a group of formula (c) or (d); the ring of formula (e) is saturated or partly or fully unsaturated, and optionally contains 1 or 2 N, O and/or S atoms and is optionally mono-, di- or trisubstituted by R<16> or mono- or disubstituted by =Q; Y = CQ or CH₂; Z = N(R<0>), Q or CH₂; A = bond, 1-8C alkanediyl, CR<2>=NNR<2>, NR<2>CQNR<2>, QCQ'NR<2>, NR<2>S(O)nNR<2>, OS(O)nNR<2>, S(O)nNR<2>, 3-12 cycloalkanediyl, C?=C, NR<2>CO, CONR<2>, NR<2>CO-5-14C arylene, O, S(O)n, 5-14C arylene, CO, CO-5-14C arylene, NR<2>, NR<2>SO₂, OCO, COO, N=CR<2> CR<2>=N, CR<2>=CR<3> or S(O)n-5-14C arylene (all optionally substituted by NR<2> and/or by 1 or 2 1-8C alkanediyl); Q, Q' = O or S; B = bond, 1-8C alkanediyl, 5-10C arylene, 3-8C cycloalkanediyl, C?=C, NR<2>, CO, CONR<2>, NR<2>CO, NR<2>-CQ-NR<2>, OCO, COO, SO, SO₂, SONR<2>, SO₂NR<2>, NR<2>SO, NR<2>SO₂, Q or CR<2>=CR<3> (all optionally mono- or disubstituted by 1-6C alkanediyl) or a divalent residue of a 5-6 membered saturated or unsaturated ring containing 1 or 2 N atoms (optionally mono- or disubstituted substituted by 1-6C alkyl or =Q); D, F = bond, 1-8C alkanediyl, 5-10C arylene, Q, NR<2>, CONR<2>, NR<2>CO, NR<2>CQNR<2>, OCO, COO, CQ, SO, SO₂, SO₂NR<2>, NR<2>SO, NR<2>SO₂, CR<2>=CR<3>, C?=C, CR<2>=NNR<2>, N=CR<2>, CR<2>=N or CHOH (all optionally mono- or disubstituted by 1-8C alkanediyl, CR<2>=CR<3> or 5-6C arylene); E = bond, 1-6C alkanediyl, 2-6C alkenediyl, 2-6C alkynediyl, phenylene, phenylene-1-3C alkanediyl or 1-3C alkanediyl-phenylene; G = CR<4>R<5>(CR<6>R<7>)p(CH₂)qR<10>; L = C(R<16>) or N; R<0> = H, 1-8C alkyl (optionally substituted by 3-12C cycloalkyl or 5-14C aryl), 1-8C alkylcarbonyl, 3-12C cycloalkylcarbonyl, (3-12C cycloalkyl- or 5-14C aryl-substituted) 1-6C alkylcarbonyl, 5-14C arylcarbonyl, 3-12C cycloalkyl or 5-14C aryl (where all alkyl are optionally substituted by 1 or more F); R<1> = NR<2>CR<2>(=NR<2>), C(=NR<2>)NR<2>R<3>, NR<2>C(=NR<2>)NR<2>R<3>, or a 4-14 membered mono- or polycyclic optionally aromatic ring (optionally containing 1-4 N, O and/or S and optionally substituted by R<12>-R<15>); R<2>, R<3> = H, 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkyl, 5-14C aryl, 5-14C aryl-1-8C alkyl, NH₂; NR<9>OR<8>, R<9>OR<8>, R<9>COOR<8>, R<9>-5-14C aryl-R<8>, R<9>N(R<8>)₂, R<9>-NR<8>-(1-8C hydroxyalkyl), R<9>CON(R<8>)₂, R<9>NR<8>COR<8>, R<9>COR<8>, C(=NR<8>)N(R<8>)₂; NR<8>C(=NR<8>)N(R<8>)₂ or (1-18C alkyl)-COO-1-6C alkoxy carbonyl; R<4>-R<7> = H, F, OH, 1-8C alkyl, 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkyl, R<9>QR<8>, R<9>OCOR<8>, R<9>COOR<8>, R<9>-5-14C aryl-R<8>, R<9>N(R<2>)R<8>, R<9>N(R<8>)₂, R<9>OCONR<8>R<2>, R<9>N(R<2>)S(O)nR<8>, R<9>NR<2>COQR<8>, R<9>NR<2>COR<8>, R<9>N(R<2>)CON(R<2>)R<8>, R<9>N(R<2>)S(O)

$n\text{NR}<2>\text{R}<8>$, $\text{R}<9>\text{S}(\text{O})n\text{R}<8>$, $\text{R}<9>\text{NR}<2>\text{COSR}<8>$, $\text{R}<9>\text{COR}<8>$, $\text{R}<9>\text{CONR}<2>\text{R}<8>$ or $\text{R}<9>\text{S}(\text{O})n\text{NR}<2>\text{R}<8>$; $\text{R}<8> = \text{H}$, 1-8C alkyl (optionally substituted by 3-12C cycloalkyl or 5-14C aryl), 3-12C cycloalkyl or 5-14C aryl (where all alkyl are optionally substituted by 1 or more F); $\text{R}<9> = \text{bond}$ or 1-8C alkanediyl; $\text{R}<10> = \text{CQR}<11>$, $\text{S}(\text{O})n\text{R}<11>$, $\text{P}(\text{O})n\text{R}<11>$ or a 4-8 membered saturated or unsaturated heterocycle containing 1-4 N, O and/or S atoms; $\text{R}<11> = \text{OH}$, 1-8C alkoxy, 5-14C aryl-1-8C alkoxy, 5-14C aryloxy, 1-8C alkylcarbonyloxy-1-4C alkoxy, 5-14C aryl-1-8C alkylcarbonyloxy-1-4C alkoxy, NH_2 , mono- or di-1-8C alkylamino, 5-14C aryl-1-8C alkylamino, 1-8C dialkylaminocarbonylmethoxy, 5-14C aryl-1-8C dialkylaminocarbonylmethoxy, 5-14C arylamino or a D- or L-amino acid; $\text{R}<12>-\text{R}<15> = \text{H}$, 1-10C alkyl (optionally substituted by one or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkyl, 5-14C aryl, 5-14C aryl-1-8C alkyl, NH_2 , $\text{R}<9>\text{OR}<8>$, $\text{R}<9>\text{COOR}<8>$, $\text{R}<9>\text{N}(\text{R}<8>)_2$, $\text{R}<9>-5-14\text{C aryl-R}<8>$; $\text{R}<9>-\text{NR}<2>$ (1-8C hydroxyalkyl), $\text{R}<9>\text{CON}(\text{R}<2>)\text{R}<8>$, $\text{R}<9>\text{N}(\text{R}<2>)\text{COR}<8>$, $\text{R}<9>\text{COR}<8>$, $\text{NR}<2>\text{C}(=\text{NR}<3>)-\text{NR}<2>\text{R}<3>$, $\text{C}(=\text{NR}<2>)\text{NR}<2>\text{R}<3>$ or Q; or 2 of $\text{R}<12>-\text{R}<15>$ which are adjacent form $-\text{OCH}_2\text{O}-$, $-\text{OCH}_2\text{CH}_2\text{O}-$ or $-\text{OC}(\text{CH}_3)_2\text{O}-$; $\text{R}<16> = \text{H}$, 1-10C alkyl optionally substituted by 1 o

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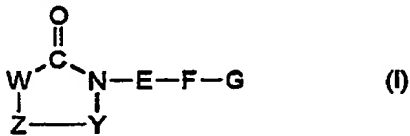
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㉖ Neue Inhibitoren der Knochenresorption und Vitronectinrezeptor-Antagonisten

㉗ Gegenstand der vorliegenden Erfindung sind 5-Ring-Heterocyclen der allgemeinen Formel I,



in der E, F, G, W, Y und Z die in den Patentansprüchen angegebenen Bedeutungen besitzen, ihre Herstellung, ihre Verwendung als Heilmittel und sie enthaltende pharmazeutische Zubereitungen. Die Verbindungen der Formel I wirken insbesondere als Vitronectinrezeptor-Antagonisten und Inhibitoren der Knochenresorption durch Osteoclasten.

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